

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended): A method of obtaining a self-renewing, phenotypically homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage, said method comprising

culturing a heterogeneous population of oligodendrocyte precursor cells having an unsynchronized developmental stage in a medium comprising an amount of a fibroblast growth factor (FGF) effective for inducing a synchronized developmental stage, and
passaging and purifying the oligodendrocyte precursor cells in the medium,

wherein said culturing is carried out in the substantial absence of platelet-derived growth factor (PDGF), thereby obtaining said self-renewing, phenotypically homogeneous population of oligodendrocyte precursor cells having a synchronized developmental stage,
wherein the FGF is FGF2, which is basic FGF or bFGF.

2. (original): The method of claim 1, wherein said self-renewing, homogeneous population of oligodendrocyte precursor cells comprises oligodendrocyte precursor cells that are culturable for at least about one year without phenotypic change in a medium comprising an amount of a fibroblast growth factor (FGF) effective to prevent said phenotypic change, and in the substantial absence of PDGF.

3. (original): The method of claim 1, wherein the cells of said heterogeneous population of oligodendrocyte precursor cells have different developmental rates in the differentiation process, produce cells of different phenotypes upon differentiation, or respond differently to environmental culturing conditions.

4. (original): The method of claim 1, wherein the cells of said homogeneous population of oligodendrocyte precursor cells have the same developmental rate in the differentiation process, produce cells of the same phenotype upon differentiation, or respond in the same manner to environmental culturing conditions.

5. (original): The method of claim 1, wherein the unsynchronized population of oligodendrocyte precursor cells comprises at least two populations of oligodendrocyte precursor cells, each having a different developmental stage, wherein said developmental stage is selected from the group consisting of the A2B5(+)O4(-)O1(-) developmental stage, the A2B5(+)O4(+)O1(-) developmental stage and the A2B5(+)O4(+)O1(+) developmental stage.

6. (original): The method of claim 1, wherein the synchronized population of oligodendrocyte precursor cells is a population of oligodendrocyte precursor cells having a A2B5(+)O4(-)O1(-) developmental stage, a A2B5(+)O4(+)O1(-) developmental stage or a A2B5(+)O4(+)O1(+) developmental stage.

7. (currently amended): The method of claim 4~~6~~, wherein said homogeneous population of oligodendrocyte precursor cells ~~are is~~ restricted to the oligodendrocyte lineage.

8. (canceled).

9. (canceled).

10. (currently amended): The method of claim 1-~~or~~9, wherein the amount of FGF is about 0.1 ng/ml to about 40 ng/ml.

11. (original): The method of claim 10, wherein the amount of FGF is about 1 ng/ml to about 10 ng/ml.

12. (currently amended): The method of claim 11, wherein the amount of ~~FGF~~bFGF is about 5 ng/ml.

13. (original): The method of claim 1, wherein the substantial absence of PDGF is an amount of PDGF less than 0.1 ng/ml.

14. (original): The method of claim 1, wherein the substantial absence of PDGF is an amount of PDGF less than 0.01 ng/ml.

15. (original): The method of claim 1, wherein the substantial absence of PDGF is an amount of PDGF less than 0.001 ng/ml.

16. (original): The method of claim 1, wherein the heterogeneous population of oligodendrocyte precursor cells is obtained from a mammal selected from the group consisting of a rodent, a human, a non-human primate, an equine, a canine, a feline, a bovine, a porcine, an ovine and a lagomorph.

17. (original): The method of claim 1, wherein the heterogeneous population of oligodendrocyte precursor cells is isolated from a member selected from the group consisting of hippocampus, cerebellum, spinal cord, cortex, striatum, basal forebrain, ventral mesencephalon, locus ceruleus, and hypothalamus.

18. (original): The method of claim 1, wherein said homogeneous population of oligodendrocytes precursor cells has at least one characteristic selected from:

- (i) ability to generate a homogeneous population of oligodendrocytes;
- (ii) ability to generate a homogeneous population of type 2 astrocytes;
- (iii) ability to dedifferentiate; and
- (iv) lack of ability to differentiate into type 1 astrocytes.

19. (withdrawn): A self-renewing, phenotypically homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage obtained by the method of claim 1.

20. (withdrawn-currently amended): A self-renewing, phenotypically homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage

obtained by the method of claim 1, wherein said homogeneous population of oligodendrocyte precursor cells ~~are~~is restricted to the oligodendrocyte lineage.

21. (withdrawn): A method of obtaining a homogeneous population of differentiated oligodendrocytes comprising culturing a self-renewing, phenotypically homogeneous population of oligodendrocyte precursor cells having a synchronized developmental stage in a medium selected from the group consisting of (a) a medium lacking any mitogens, (b) a medium comprising an amount of ciliary neurotrophic factor (CNTF) sufficient to induce differentiation of said oligodendrocyte precursor cells, (c) a medium comprising an amount of a 3,3',5'-triiodothyronine (T3) sufficient to induce differentiation of said oligodendrocyte precursor cells, and (d) a medium comprising an amount of ciliary neurotrophic factor (CNTF) and an amount of 3,3',5'-triiodothyronine (T3) sufficient to induce differentiation of said oligodendrocyte precursor cells.

22. (withdrawn): The method of claim 21, wherein the amount of CNTF is about 1 ng/ml to about 20 ng/ml.

23. (withdrawn): The method of claim 21, wherein the amount of T3 is about 1 µg/ml to about 30 µg/ml.

24. (currently amended): A method of maintaining an undifferentiated population of oligodendrocyte precursor cells in culture comprising:

culturing an undifferentiated population of oligodendrocyte precursor cells in a medium comprising an amount of a fibroblast growth factor (FGF) effective for maintaining an undifferentiated developmental stage, and

passaging and purifying the oligodendrocyte precursor cells in the medium,

wherein said culturing is carried out in the substantial absence of platelet-derived growth factor (PDGF), thereby maintaining an undifferentiated population of oligodendrocyte precursor cells in culture,

wherein the FGF is FGF2, which is basic FGF or bFGF.

25. (canceled).

26. (canceled).

27. (currently amended): The method of claim 24 ~~or~~ 26, wherein the amount of FGF is about 0.1 ng/ml to about 40 ng/ml.

28. (original): The method of claim 27, wherein the amount of FGF is about 1 ng/ml to about 10 ng/ml.

29. (currently amended): The method of claim 28, wherein the amount of ~~FGF~~ bFGF is about 5 ng/ml.

30. (original): The method of claim 24, wherein the substantial absence of PDGF is an amount of PDGF less than 0.1 ng/ml.

31. (original): The method of claim 24, wherein the substantial absence of PDGF is an amount of PDGF less than 0.01 ng/ml.

32. (original): The method of claim 24, wherein the substantial absence of PDGF is an amount of PDGF less than 0.001 ng/ml.

33. (withdrawn): A method of dedifferentiating a self-renewing, phenotypically homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage comprising: culturing a self-renewing, phenotypically homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage in a medium comprising at least one growth factor in an amount effective to promote dedifferentiation.

34. (withdrawn): The method of claim 33, wherein said homogenous population of oligodendrocyte precursor cells has an A2B5(+)O4(+)O1(+) developmental stage, and said at least one growth factor is bFGF in an amount of about 0.1 ng/ml to about 40 ng/ml.

35. (withdrawn): The method of claim 33, wherein said homogenous population of oligodendrocyte precursor cells has an A2B5(+)O4(+)O1(-) developmental stage, and said at least one growth factor is PDGF in an amount of about 1 ng/ml to about 50 ng/ml.

36. (withdrawn): The method of claim 34, wherein said medium further comprises PDGF in an amount of about 1 ng/ml to about 50 ng/ml and neutrophin-3 in an amount of about 1 ng/ml to about 10 ng/ml.

37. (withdrawn): The method of claim 35, wherein said medium further comprises bFGF in an amount of about 0.1 ng/ml to about 40 ng/ml and neutrophin-3 in an amount of about 1 ng/ml to about 10 ng/ml.

38. (withdrawn): The method of claim 33, wherein the homogeneous population of oligodendrocyte precursor cells is a homogeneous population of oligodendrocyte precursor cells having an A2B5(+)O4(-)O1(-) developmental stage, an A2B5(+)O4(+)O1(-) developmental stage or an A2B5(+)O4(+)O1(+) developmental stage.

39. (withdrawn): The method of claim 33, wherein the homogeneous population of oligodendrocyte precursor cells dedifferentiate into a homogeneous population of oligodendrocyte precursor cells having an A2B5(+)O4(-)O1(-) developmental stage or an A2B5(+)O4(+)O1(-) developmental stage.

40. (withdrawn): The method of claim 33, wherein the dedifferentiated oligodendrocyte precursor cells can differentiate into oligodendrocytes or into type 2 astrocytes.

41. (withdrawn): The method of claim 33, further comprising transferring said oligodendrocyte precursor cells at least once during said culturing step by cell dissociation using a digestive reagent.

42. (withdrawn): A population of dedifferentiated oligodendrocyte precursor cells obtained by the dedifferentiation method of claim 33.

43. (withdrawn): A self-renewing, phenotypically homogeneous population of oligodendrocyte precursor cells having a synchronized developmental stage that differentiates into type 2 astrocytes in response to treatment with bone morphogenic protein 2 (BMP-2) or BMP-4 in an amount effective to induce differentiation into type 2 astrocytes but not in response to treatment with any amount of ciliary neurotrophic factor (CNTF).

44. (withdrawn): A dedifferentiated, homogeneous population of oligodendrocyte precursor cells that differentiates into type 2 astrocytes in response to treatment with bone morphogenic protein 2 (BMP-2) or BMP-4 in an amount effective to induce differentiation into type 2 astrocytes but not in response to treatment with any amount of ciliary neurotrophic factor (CNTF).

45. (withdrawn): The method of claim 43 or 44, wherein the amount of BMP-2 and BMP-4 is about 1 ng/ml to about 20 ng/ml.

46. (withdrawn): A method of screening for compounds that affect a biological function of a homogeneous population of oligodendrocyte precursor cells, a population of oligodendrocytes or a population of type 2 astrocytes, comprising:

- (a) contacting a self-renewing, phenotypically homogeneous population of oligodendrocyte precursor cells having a synchronized developmental stage obtained by the method of claim 1 or a population of oligodendrocytes differentiated from said homogeneous population obtained by the method of claim 1 or a population of type 2 astrocyte differentiated from said homogeneous population obtained by the method of claim 1 with a test compound; and
- (b) detecting a change in a biological function of the oligodendrocyte precursor cells, the oligodendrocytes or the type 2 astrocytes.

47. (withdrawn): The method of claim 46, wherein said homogeneous population of oligodendrocyte precursor cells is a population selected from the group consisting of oligodendrocyte precursor cells of the A2B5(+)O4(-)O1(-) developmental stage, oligodendrocyte precursor cells of the A2B5(+)O4(+)O1(-) developmental stage and oligodendrocyte precursor cells of the A2B5(+)O4(+)O1(+) developmental stage.

48. (withdrawn): The method of claim 46, wherein the change is an increase or reduction in at least one of the characteristics selected from the group consisting of myelination, differentiation into oligodendrocytes or type 2 astrocytes, proliferation speed, cell migration, viability, gene expression, protein expression, protein levels in the culturing medium, dedifferentiation, growth characteristics, and cell morphology.

49. (withdrawn): A method of treating a patient with a disease or condition affecting the central nervous system, comprising administering to the patient a therapeutically effective amount of a self-renewing, phenotypically homogeneous population of oligodendrocyte precursor cells having a synchronized developmental stage obtained by the method of claim 1.

50. (withdrawn): The method of claim 49, wherein said oligodendrocyte precursor cells are differentiated or dedifferentiated prior to administration to said patient.

51. (withdrawn): The method of claim 49, wherein said disease or condition is a demyelinating disease or a neurodegenerative disease.

52. (withdrawn): The method of claim 51, wherein said demyelinating disease is selected from the group consisting of spinal cord injury (SCI), multiple sclerosis (MS), human immunodeficiency MS-associated myelopathy, transverse myelopathy/myelitis, progressive multi focal leukoencephalopathy, and central pontine myelinolysis lesions to the myelin sheathing.

53. (withdrawn): The method of claim 51, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer disease, senile dementia of Alzheimer type (SDAT), Parkinson disease, Huntington disease, ischemia, blindness, and a neurodegenerative disease due to myelinated neuron injury.

54. (withdrawn): A substantially pure culture of rat A2B5(+)O4(+)O1(-) self-renewing oligodendrocyte precursor cells having ATCC deposit number PTA 6093.

55. (withdrawn): A substantially pure, self-renewing homogenous population of oligodendrocyte precursor cells having a synchronized developmental stage.

56. (withdrawn): The oligodendrocyte precursor cells of claim 55, wherein said synchronized developmental stage is A2B5(+)O4(-)O1(-).

57. (withdrawn): The oligodendrocyte precursor cells of claim 55, wherein said synchronized developmental stage is A2B5(+)O4(+)O1(-).

58. (withdrawn): The oligodendrocyte precursor cells of claim 55, wherein said synchronized developmental stage is A2B5(+)O4(+)O1(+).

59. (withdrawn): The oligodendrocyte precursor cells of claim 55, wherein said synchronized developmental stage is bFGF dependent.

60. (withdrawn): An admixture of a substantially pure, self-renewing homogenous population of oligodendrocyte precursor cells consisting of at least two different synchronized developmental stages, wherein said developmental stage is selected from the group consisting of the A2B5(+)O4(-)O1(-) developmental stage, the A2B5(+)O4(+)O1(-) developmental stage, and the A2B5(+)O4(+)O1(+) developmental stage.

61. (new): The method of claim 1, wherein the medium further comprises 3, 3',5'-triiodothyronine (T3).

62. (new): The method of claim 1, wherein the heterogeneous population of oligodendrocyte precursor cells is harvested from spinal cord.

63. (new): The method of claim 24, wherein the medium further comprises 3, 3',5'-triiodothyronine (T3).

64. (new): The method of claim 24, wherein the heterogeneous population of oligodendrocyte precursor cells is harvested from spinal cord.